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RE: Joint Meeting of the Blood Products Advisory Committee and the Microbiology Devices Panel of the Medical Devices Advisory Committee; Notice of Meeting; Request for Comments

Dear Drs. Shuren and Marks:

The Infectious Diseases Society of America (IDSA) and HIV Medicine Association (HIVMA) would like to thank the Food and Drug Administration (FDA) for scheduling a joint meeting of the Blood Products Advisory Committee and the Microbiology Devices Panel of the Medical Devices Advisory Committee. This joint meeting will discuss reclassification of diagnostic tests for Human Immunodeficiency Virus (HIV) and hepatitis C virus (HCV) devices from Class III (Premarket approval or PMA) to Class II (510(k)). We urge the FDA to classify these viral diagnostic tests as Class II.

For years, IDSA has stressed the need for innovative diagnostic devices to improve care for patients at risk for or suffering from infectious diseases (ID). In 2013, the Society issued a dedicated report: Better Tests, Better Care: Improved Diagnostics for Infectious Diseases. The principles outlined in the report should be applied for both HIV and HCV diagnostics. More than 1.2 million Americans are living with HIV, but greater than 10% are unaware of their infection. Infections are increasingly seen in adolescents and young adults who are often not engaged in routine medical care. Vulnerable populations also lack resources, medical insurance, and transportation to pursue definitive testing in physician offices. Return visits to a testing center for confirmatory assessments are particularly challenging for many. Such barriers could be removed by improved technologies allowing for conclusive point of care testing. This would lead to a more significant proportion of people with HIV infection achieving a diagnosis and entering treatment.

Earlier diagnosis of HIV is critical since later recognition means the onset of profound immunodeficiency with AIDS and opportunistic infections that lead to worse outcomes and increased mortality. An additional benefit of earlier diagnosis and treatment means control of viral replication with effective medication, thus reducing the transmission potential in treated individuals. Point of care testing and improved third- and fourth-generation serologic HIV testing have transformed the diagnostic armamentarium. Continued advances in these technologies and enhanced availability are critical to meet evolving clinical needs.

The same scenarios are true for HCV diagnostic tests. Risk factor identification for HCV has not been exceptionally successful in identifying the majority of people with this often silent infection. More than 75% of infected adults are baby boomers or people born from 1945 through 1965. Most people with HCV do not know they are infected because they are not clinically ill unless the disease progresses to cirrhosis or liver cancer[1]. Treatment of HCV has undergone a therapeutic revolution in the past five years. The oral, state of the art drugs available for treatment now allow for shorter treatment duration and high rates of sustained virologic response compared to older, interferon-based therapies. HCV genotyping allows clinicians to determine the best treatment regimens, especially in patients who have failed prior treatments. Scientists believe we can end the HCV epidemic with this curative therapy if people with HCV can be diagnosed and then treated at high numbers that would then stop transmission. IDSA and HIVMA believe that categorizing HCV tests as Class III, or high risk, is inappropriate and limits the development of improved tests. We encourage FDA to reclassify HCV viral load tests, HCV genotyping tests, and point-of-care (POC) and laboratory-based tests for the diagnosis of HIV as Class II devices.

Diagnostic tests for HIV and HCV: routinely used, well supported by the literature, risks easily mitigated

The management of HIV and HCV is routine for ID specialists. Diagnostic tests for HIV and HCV have been in use for many years by clinical laboratories with well-documented data demonstrating their clinical validity and peer reviewed literature supporting their use. The efficacy and acceptability of rapid, POC HIV antibody tests have been demonstrated with over a decade of studies and cost analyses that show rapid POC testing as cheaper per delivered test result when compared with standard blood testing.[2] Assay standardization and clinical studies for patients with HIV and HCV have led to robust expert guidelines for testing and managing these patients.

The risk associated with HIV and HCV diagnostic testing is further mitigated by additional factors. For HIV, confirmatory testing (also a serologic test) limits the possibility of false positive results. Further quantitative viral PCR testing peformed for judging therapeutic efficacy, while not approved for diagnosis, gives additional information that if inconsistent with the diagnostic results allows the clinician to identify potentially rare, unusual cases that may require additional testing to confirm or refute the diagnosis. Similarly, HCV genotype testing done before selecting drug therapy would confirm the viral infection. Clinicians also use several additional factors to inform clinical decisions. For example, a clinician will assess pathology, patient history, and other data in a clinical context to optimally manage a patient.

More significant risk to patient care posed by Class III designation

[1] CDC. "Screening in Hospital Emergency Room Finds Baby Boomers with Hepatitis C." Available at: https://www.cdc.gov/nchhstp/docs/successstories/hcv-in-er-al.pdf.

[2] ML Schito et al. Challenges for rapid molecular HIV diagnostics. The Journal of Infectious Diseases, Volume 201, Issue Supplement_1, 15 April 2010, Pages S1–S6, https://doi.org/10.1086/650394

IDSA also encourages the panel and the FDA to consider the risks posed by classifying these tests as Class III, or high risk—namely, significantly diminished patient access to testing. A Class III designation requires developers to submit a PMA for any new commercial test. The associated costs often deter much-needed innovation that would lead to improvements in clinical care. A PMA requires multi-million-dollar, multi-site clinical trials that often require many years to complete. This regulatory process swells costs that could equal or surpass the pre-clinical research and development costs that alone can range from $20 million to $100 million per device. A reclassification of HIV and HCV diagnostic testing to Class II (510(k) clearance process) should lead to a significant reduction in clinical trial costs, faster time to market, and therefore encourage commercial companies to invest in new approaches that lead to FDA clearance. More FDA cleared devices would give laboratories options when selecting the device best suited for their testing and clinical needs.

HIV diagnosis requires two tests: a serologic screening test (which can be POC) and a follow-up confirmatory test, which is most commonly a laboratory-based test. There is neither a CLIA-waived/POC confirmatory HIV differentiation assay recommended as a confirmatory test in the U.S., nor an approved fourth generation confirmatory test to confirm acute infection. Easing the developmental pathway would allow companies to develop molecular assays that would diagnose HIV in point-of-care fashion both for screening and for confirmation. If such tests were widely available, both patient access and follow-up would benefit.

For HCV, the ideal POC test is minimally invasive and would use saliva or finger-prick blood as a primary sample. Such a test would yield accurate, rapid results that differentiate between active infection from the 10-20% of individuals who have cleared the viral infection through their native immune repsonse. It should also be portable and self-contained leading to use in areas without infrastrucutre as well as working at low cost. To date, except for anti-HCV antibody testing, no such POC test is currently available.[3]"

FDA states that Class III devices can be downclassified to Class II when sufficient information becomes available to establish special controls that reasonably assure safety and effectiveness. A change from Class III to Class II will not change the rigor applied to the analytical performance of the tests that is predetermined whether the test is a Class II or III. Therefore, test performance should not be of concern in this decision process. What does change is the degree of clinical study that is needed. Class II allows comparison to an existing test in clinical study. Class III requires clinical studies that define the test utility. Clinical studies for Class III tests are more complicated and costly. They should not be necessary if the utility of tests has already been substantially established with numerous clinical studies.

Removing Class III regulatory barriers for these well-characterized HIV and HCV tests would spur new and better technologies by companies that are interested in developing molecular tests with a faster pathway U.S marketing approval. Additionally, many commercially available HCV tests are performed using the same instruments as those used to test for HIV. Consideration should be given to testing approaches that would jointly tackle the challenges presented by these often-overlapping pandemics.

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[3] J. Clin. Microbiol. February 2016 vol. 54 no. 2 265-273.

Conclusion

The current high-risk classification for HIV and HCV diagnostic tests is an excessively high bar requiring any new test to undergo costly and burdensome PMA submission. Reclassifying HIV and HCV diagnostics as Class II or moderate risk devices should increase the number of commercial tests submitted for FDA clearance. This will likely prompt innovation that will lead to greater availability of these tests and improved patient care over a larger population.

Given their longstanding use and significant supporting data, diagnostic tests for HIV and HCV do not pose a high risk to patients and should be classified as Class II or moderate risk tests.

IDSA and HIVMA much appreciate the opportunity to provide comments on this vital issue. Should you have any questions or concerns about these comments, please feel free to contact Jaclyn Levy, IDSA Senior Program Officer for Science and Research Policy, at jlevy@idsociety.org or 703-299-1216. We look forward to continued dialogue with the FDA to guide policymaking in this area.

Sincerely,

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President, IDSA

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Chair, HIVMA Board of Directors